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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,634	12/14/2001	Ronenn Roubenoff	21629-004	1772

7590 09/09/2005

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,634	ROUBENOFF ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.02

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114. Claims 1-13 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claim 1-13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Muller et al. (US 6011040) in view of Smith et al. (WO 98/19690).

Muller expressly teaches a composition comprising reduced folate compound (i.e., 5-formimino-(6S)-tetrahydrofolic acid and vitamin B (i.e., vitamin B12), wherein an amount of said reduced folate compound is in dose range between 0.001mg and 1000mg, and an amount of said vitamin B12 is in dose range of 0.001mg and 0.5mg (column 2, lines 19-25; column 3, lines 9-21 and lines 30-40; Example 10; claims 5, 19-20).

Smith expressly teaches a composition, which is useful in treating Alzheimer's disease or occlusive vascular diseases, comprising (i) folic acid, betaine and vitamin B12 or (ii) folate or folate derivatives (e.g., tetrahydrofolic acid, 5,10-methylenetetrahydrofolate, 5-methyltetrahydrofolate, 5,10-methyenyltetrahydrofolate, 5-fomyltetrahydrofolate, etc...), betaine and vitamin B12, wherein said composition can be prepared in single fixed combination such as single tablet or single capsule (page 4, line 34 thru page 5, line 20; page 10, lines 3-6; page 11, lines 3-9; Example 1; claims 25 and 27). Smith also expressly teaches that (i) the folic acid or folate or derivatives is employed in a weight ratio to vitamin B12 of within the range from about 0.1:1 to about 50:1 and preferably from about 0.2:1 to about 25:1 (column 6, lines 5-8); and (ii) the folic acid or folate or derivative or betaine is employed in daily oral doses within the range from about 0.1 to about 100mg, preferably from about 2 to about 10mg, and vitamin B12 is employed in daily oral doses within the range from about 0.001 mg to abut 10mg, preferably from about 0.5 to about 2.5mg (column 6, lines 41-47).

The teaching of the cited references in combination differs from the claimed invention in (i) the use of a natural isomer of reduced folate (e.g., (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic aicd, etc...) for preparing said composition; and (ii) the specific ratio of the folate compound and the cobalamin is 125:1.

One having ordinary skill in the art would have expected that the individual isomers are obvious variants over the corresponding racemate because of their presence in the racemate. It would further be expected that one of the isomers would be more active than the other and the racemate would exhibit the combined effects. Thus, one having ordinary skill in the art would have been motivated to employ a natural isomer of reduced folate such as (e.g., (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic aicd, etc...) to arrive at the claimed composition such that the pharmacological activity of said composition would be greatly enhanced.
In addition, those of ordinary skill in the art would have readily optimized effective dosage ratio in light of Muller who teaches the ratio of reduced folate to cobalamin as 200:1 (see Example 10) and Smith who teaches the ratio of reduced folate to cobalamin between 0.1:1 and 50:1. One having ordinary skilled in the art would have expected that optimization of said ratio between 0.1:1 to 200:1 is old and well known.

Conclusion

3. No Claim is allowed.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614